5,25

CXCR4, CD4, CCR5 (not expressed well) BONZO CD4, low level expression of CCR5 and CXCR4 Receptor CD4, CXCR4, CCR5 CD4, CXCR4, CCR5 HOS.CD4.CCR5.GFP.M7#6*CD4, CXCR4, CCR5 CD4, CXCR4, CCR5 CD4, CCR5, BONZO CD4, CXCR4, CCR5 Cells CD4, CXCR4 CD4, CXCR4 CD4, CXCR4 CD4, CXCR4 CD4, CCR5 CD4, CCR5 CD4 HOS HT4 R5 GFP wt HOS.CD4.CXCR4 **CEM NKr CCR5** HOS.CD4.CCR5 Ce 5.25.Luc4.M7 **J87.CD4 R5 U87.CD4 X4** HOS.CD4 P4.CCR5 **J87.CD**₫

MT2

MT4

PM1

 Table 2
 Representative viruses and reagents

177597543750000000000000000000000000000000000	Envelope :	
89.6, SF2	R5-X4/SI/B	ARRRP ^B
92BR014,92US076	R5-X4/SI/B	ARRRP
JR-CSF, 91US005	R5/NSI/B	ARRRP
91US054	SI/B	ARRRP
NL43, MN, ELI	X4/B	ARRRP
92HT599	X4	ARRRP
92UG031	R5/NSI/A	ARRRP(IN-HOUSE)
92TH014, 92TH026	R5/NSI/B	ARRRP(IN-HOUSE)
92BR025, 93MW959	R5/SI/C	ARRRP(IN-HOUSE)
92UG035	R5/NSI/D	ARRRP(IN-HOUSE)
92TH022, 92TH023	R5/NSI/E	ARRRP(IN-HOUSE)
93BR020	R5-X4/SI/F	ARRRP(IN-HOUSE)
Antipodies	Epitope	SOURCE
Mabs 2F5, 1577	gp41 TM	ARRRP
Mabs IG1b12, 2G12, 17b, 48D	gp120 SU	ARRRP
Neutralization sera #2, HIV-	Polyclonal	ARRRP
IG		
Entry inhibitors	Target	Source
CD4-TG	gp120 SU	Genentech
CD4-IGG2	gp120 SU	Adarc
SCD4	Sigma	Progenics
T20 (DP178)	gp41 TM	Trimeris
Rantes, MIP1a/b	CCR5	SIGMA/ARRRP
SDF1a/b	CXCR4	SIGMA/ARRRP
AMD 3100	CXCR4	AnorMed
Dextran sulfate, Heparin	Non-specific	Sigma

aR5 (CCR5 co-receptor), X4 (CXCR4 co-receptor)

SI (syncytium inducing), NSI (non-syncytium inducing), A,B,C,D,E,F (envelope clade designation)

bAIDS Research and Reference Reagent Program

Primers Tested for the Amplification of HIV Envelope

RT PRIMERS

RT env_N3 RT env 9720

5'-GGA GCA TTT ACA AGC AGC AAC ACA GC-3'

RT env 9740

5' -TTC CAG TCA VAC CTC AGG TAC-3' 5'-AGA CCA ATG ACT TAY AAG G-3'

5' PCR PRIMERS

5'env

5' -GGG CTC GAG ACC GGT CAG TGG CAA TGA GAG TGA AG- 3'

5'env_Xho/Pin 5'-GGG CTC GAG ACC GGT GAG CAG AA-3 ACA GTG GCA ATG A-3' 5'env_START 5'-GGG CTC GAG ACC GGT GAG CAG AAG ACA GTG GCA ATG -3'

3' PCR PRIMERS

3' env

1,2 1 2 m

5' -GGG TCT AGA ACG CGT TGC CAC CCA TCT TAT AGC AA- 3' 3'env_Xba/Mlu 5'-GGG TCT AGA ACG CGT CCA CTT GCC ACC CAT BTT ATA GC-3'

3'env_STOP

5'-GGG TCT AGA ACG CGT CCA CTT GCC ACC CAT BTT A-3'

3' delta CT

5' -GAT GGT CTA AGA CGC TGT TCA ATA TCC CTG CCT AAC TC- 3'

All Experiments are located in Virologic Book number 0188

Table 4 (Panel 1)

Anti-HIV	Drugs
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	Anti-	HIV Drugs	
Drug/Compound	Generic Name	Trademark	Manufacturer
RT Inhibitors (NRTI, nucleotide anal			202
AZT, ZDV	Zidovudine	Retrovir	Glaxo/Wellcome
3TC	Lamivudine	Epivir	Glaxo/Wellcome
AZT + 3TC	Lamvadise	Combivir	Glaxo/Wellcome
d4T	Stavudine	Zerit	Bristol-Myers/Squibb
ddl	Didanosine	Videx	Bristol-Myers/Squibb
ddC	Zalcitabine	Hivid	Hoffman La Roche
1592U89	Abacavir	Ziagen	Glaxo/Wellcome
AZT + 3TC + 1592U89	715000111	Trizivir	Glaxo/Wellcome
(-)FTC (5-fluoro-3TC; Corviracil)	Emtricitabine		Triangle Pharmaceuticals
(-)FTC + (+)FTC (50:50)	Racimir		QuadPharma
DAPD (DXG active)	Amdoxovir		Triangle Pharmaceuticals
F-ddA (2-fluoro-ddA)	Lodenosine		MedImmune Oncology (US Bioscience)
BCH-10652, dOTC	Loculosino		BioChem Pharma, Inc.
(2-deoxy-3-oxa-4-thiocytidine)			Disconstill Hamile, mo.
D-d4FC			Triangle Pharmaceuticals (Schinazi)
RT Inhibitors (NTRT), nucleotide and	alogs)	1	Thango Hamacaataa (Commany
bis-POC PMPA (GS-4331)	Tenofovir	T	Gilead Sciences
bis-POC PMPA (GS-4331) bis-POM PMEA (GS-840)	Adefovir dipivoxil	 	Gilead Sciences
RT Inhibitors (NNRT), non-nucleosid		1	
BI-RG-587	Nevirapine	Viramune	Boehringer/Ingleheim (Roxanne)
BI-RG-587 BHAP PNU-90152T	Delavirdine	Rescriptor	Pharmacia & Upjohn
	Efavirenz	Sustiva	Dupont Pharmaceuticals (Avid)
DMP 266 (L-743,726)	Emivirine	Sustiva	Triangle/Mitsubishi Kasei
MKC442 (Coactinon)			Agouron Pharmaceuticals
AG-1549 (S1153) (on hold)	Capravirine		Pharmacia & Upiohn
PNU-142721			DuPont Pharmaceuticals
DPC-961, -963, -083, -08?	Alexander inhihitana		Samjin Pharmaceuticals
SJ-3366	Also entry inhibitor?		
BHAP PNU-87201	Atevirdine	 	Upjohn Glaxo/Wellcome (Hoechst Bayer)
GW420867X (quinoxaline)	(2 nd gen. HBY 097)	ļ	Tibotec
TMC 120 (R147681)			Tibotec
TMC 125 (R165335)			Janssen Pharmaceuticals
R86183	tivirapine		
Calanolide A			Sarawak Medichem Pharmaceuticals
Protease Inhibitors (PRI)		Invirase	Hoffman-La Roche
Ro 31-8959	Saquinavir-(hgc) Saquinavir-(sgc)	Fortivase	Hollinan-La Roche
MIX 620 (1 725 524)	Indinavir	Crixivar.	Merck Research Laboratories
MK-639 (L-735,524)	Ritonavir	Norvir	Abbott Laboratories
ABT-538 (A-84538)	Nelfinavir	Viracept	Agouron Pharmaceuticals
AG1343	Amprenavir	Agenerase	Glaxo-Wellcome/Vertex
141W94 (VX-478) ABT-378/r	Lopinavir/ritonavir	Kaletra	Abbott Laboratories
	Lopinavii/Ittoriavii	Naieua	Bristol-Myers-Squibb
BMS 232,632 (aza-peptide) PNU-140690	Tipranavir		Pharmacia & Upjohn
DMP 450 (cyclic urea)	Mozenavir		Triangle/Avid (ph I/II)
TMC 126 (Erickson's compound)	Mozeriavii		Tibotec
	amprenavir pro-drug		Glaxo/Wellcome/Vertex
G/W433908 (VX-175) L756,423 (on hold)	ampiellavii piu-ulug		Merck
PD-178390 (dihydropyrone)		 	Parke Davis (Boehringer-Ingleheim)
		 	Roche
? new candidate DPC 681 and 684			DuPont Pharmaceuticals
AG-1776 (JE-2147 = KNI-764)			Agouron Pharmaceuticals
			Agodion Pharmaceuticals
	Pentafuside		Trimeris Pharmaceuticals
T-20 (gp41)			Trimeris Pharmaceuticals
T-1249 (gp41)	I. SCH-C		Schering-Plough
D-peptide inhibitor (gp41) small mo			AnorMED
AMD-3100 (CXCR4)	(bicyclam)		AnorMED
AMD-8664 (CXCR4)	(macrocyclam)	+	U. PA
ALX40-4C (CXCR4)		 	
FP21399	1001165		Fuji Pharmaceuticals
PRO 542 (gp120)	CD4lgG2		Progenics Pharmaceuticals
PRO-140 (CCR5)	MAb CCR5		Progenics Pharmaceuticals
T-22 (CXCR4)	(peptide, 18-mer)		
Met-SDF-1 (CXCR4)			
TAK 779 (CCR5 antagonist)			Takeda
AOP-Rantes (CCR5)		1	Gryphon Sciences

Table 4 (Panel 2)

Rantes 9-68 (CCR5)		
CCR5 antagonists	4-(piperidin-1-yl) butane class	Merck
α-Immunokine-NNS03 (CCR5, CXC	R4) α-cobratoxin	PhyloMed Corp.
Integrase Inhibitors	And the second s	
AR-177	Zintevir	Aronex Pharmaceuticals
Diketo acids		Merck Research Laboratories
Nucleocapsid Inhibitors		
RB 2121	cyclic peptide p7 mimic	(see PNAS 96:4886-4891 (1999))
CI-1012		Achelion Pharmaceuticals
RNase H Inhibitor	The Company of the Co	
SP1093V (BBNH Fe+3 derivative)		(Parniak)

FDA approved drugs are shown in boldface red = discontinued development, blue = not sure about development status

Table 4 (Panel 3

Firm

Generic Name (abbreviation) zidovudine, AZT didanosine, ddl zalcitabine, ddC stavudine, d4T lamivudine, 3TC saquinavir, SQV, hgc saquinavir, SQV, sgc ritonavir. RTV indinavir, IDV nevirapine, NVP nelfinavir, NFV delavirdine. DLV ZDV+3TC efavirenz, EFV abacavir, ABC amprenavir lopinavir/ritonavir ZDV+3TC+ABC

Brand Name Retrovir Videx Hivid Zerit **Epivir** Invirase Fortovase Norvir Crixivan Viramune Viracept Rescriptor Combivir Sustiva Ziagen Agenerase Kaletra

Trizivir

Glaxo Wellcome Bristol Myers-Squibb Hoffman-La Roche Bristol Myers-Squibb Glaxo Wellcome Hoffman-La Roche Hoffman-La Roche Abbott Laboratories Merck & Co., Inc. Boehringer Ingelheim Agouron Pharmaceuticals Pharmacia & Upjohn Glaxo Wellcome **DuPont Pharmaceuticals** Glaxo Wellcome Glaxo Wellcome Abbott GlaxoSmithKline

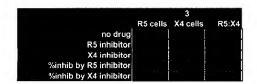
Date March 87 October 91 June 92 June 94 November 95 December 95 November 97 March 96 March 96 June 96 March 97 April 97 September 97 September 98 February 99 April 99 September 2000 November 2000

FDA Approval

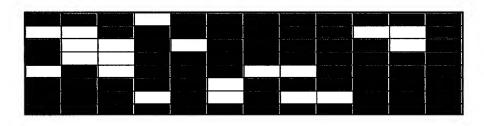


CORECEPTOR ASSAY SCREEN TEMPI ATF

CORE	CEPTO	R ASS	AYSC	REEN	TEMP	LATE							drug 1: I	83				
active	RLU limit:	100		tropism r	atıo limit:	5		CXCR4	CCR5	DUAL			drug 2: /					
No Drug RLU L83 RLU AMD RLU	R5 34	1 X4 26,471 19,258 32	R5:X4 0 00	R5 14,140 54 12,186	2 X4 55	R5:X4 257 09	R5 46	3 X4 6,849 4,696 40	R5:X4 0 01	R5 21,656 27 7,226	X4 38,144 25,542 32	R5:X4 0 57	R5 30	5 X4 7,336 5,468 39	R5:X4 0 00	R5 3,988 34 3,664	6 X4 31	R5:X 128 6
No Drug RLU L83 RLU AMD RLU	R5 4,552 28 838	13 X4 19,102 9,956 34	R5:X4 0 24	R5 149 40 41	14 X4 226 153 24	R5:X4 0 66	R5 67,389 99 42,295	15 X4 72	R5:X4 935 96	R5 611 30 76	16 X4 19,715 14,985 1,022	R5:X4 0 03	R5 46	17 X4 3,948 2,953 152	R5:X4 0 01	R5 284 38 25	18 X4 4,330 2,918 48	R5:X
No Drug RLU L83 RLU AMD RLU	R5 67,828 129 51,146	X4 68	R5:X4 997.47	R5 14,982 111 8,580	X4 12,020 10,839 3,384	R5:X4 1 25	R5 3,788 59 2,049	X4 4,384 3,397 538	R5:X4 0 86	R5 50	. X4 . 37	R5:X4	R5 658 32 493	29 X4 242 221 38	R5:X4 2 72	R5 231 47 219	30 X4 35	R5:X
No Drug RLU L83 RLU AMD RLU	R5 100	39 49	R5:X4	R5 3,724 38 1,984	2,310 2,656 272	R5:X4 1 61	R5 450 37 206	X4 668 463 72	R5:X4 0 67	R5 148 33 139	40 X4 24	R5:X4 6.17	R5 32	41 X4 22	R5:X4	R5 60	42 X4 61	R5:X
No Drug RLU L83 RLU AMD RLU	R5 35	X4 107 68 34	R5:X4 0 33	R5 83	50 X4 4,209 3,502 88	R5:X4 0.02	R5 18,099 13,896 16,980	51 X4 8,451 6,220 8,711	R5:X4 2 14	R5 39,257 85 27,832	52 X4 38	R5:X4 1033,08	R5 5,413 35 5,043	53 X4 40	R5:X4 135 33	R5 97,733 30 48,452	54 X4 29	R5:X 3370 1
No Drug RLU L83 RLU AMD RLU	R5 3,769 29 2,773	61 X4 40	R5:X4 94 23	R5 786 39 797	62 X4 48	R5:X4 16 38	R5 340 31 282	63 X4 21	R5:X4 16 19	R5 5,189 34 5,356	64 X4 43	R5:X4 120 67	R5 4,318 28 3,461	65 X4 37	R5:X4 116 70	R5 196 23 184	66 X4 51	R5:X 3 8
No Drug RLU L83 RLU AMD RLU	R5 391 50 340	73 X4 26	R5:X4 15 04	R5 98	74 X4 38	R5:X4	R5 4,449 43 3,752	75 X4 28	R5:X4 158,89	R5 4,357 34 906	76 X4 9,102 7,932 36	R5:X4 0 48	R5 6,090 73 4,473	77 X4 105 77 51	R5:X4 58 00	R5 1,886 38 279	78 X4 3,635 2,092 27	R5:X 0 5
No Drug RLU L83 RLU AMD RLU	R5 510 42 564	85 X4 33	R5:X4 15 45	R5 979 55 813	86 X4 59	R5:X4 16 59	R5 491 49 376	87 X4 33	R5:X4 14 88	R5 300 29 268	88 X4 3,815 3,661 36	R5:X4 . 0 08	R5 297 32 256	89 X4 3,615 2,946 30	R5:X4 0 08	R5 39	90 X4 61,594 56,739 40	R5:X 0.0
	,																	
No Drug RLU L83 RLU AMD RLU	R5 30	7 X4 1,217 814 42	R5:X4 0.02	R5 49	8 X4 1,128 934 37	R5:X4 0.04	R5 42,206 90 33,192	9 X4 70	R5:X4 602 94	R5 45	10 X4 1,159 761 33	R5:X4 0 04	R5 44,589 60 30,510	11 X4 97	R5:X4 459 68	R5 32	12 X4 29,118 22,279 31	R5:X
No Drug RLU L83 RLU AMD RLU	R5 100	19 X4 5,204 3,058 34	R5:X4 0 02	R5 11,299 22 8,232	20 X4 52	R5:X4 217.29	R5 1,273 26 1,129	21 X4 20	R5:X4 63 65	R5 7,375 40 3,961	22 X4 10,856 6,455 2,283	R5:X4 0 68	R5 4,397 42 1,656	23 X4 7,130 3,874 1,285	R5:X4 0 62	R5 16,115 68 11,980	24 X4 50	R5:X 322.3
No Drug RLU L83 RLU AMD RLU	R5 53	31 X4 974 828 95	R5:X4 0.05	R5 177 32 361	32 X4 32	R5:X4 5.53	R5 24,739 31 21,767	33 X4 33	R5:X4 749.67	R5 612 48 479	34 X4 45	R5:X4 13 60	R5 2,997 22 925	35 X4 9,695 7,261 35	R5:X4 0 31	R5 416 28 597	36 X4 31	R5:X -13.4:
No Drug RLU L83 RLU AMD RLU	R5 45	43 X4 338 207 29	R5:X4 0.13	R5 714 31 366	44 X4 45	R5:X4 15 87	R5 11,029 18 8,390	45 X4 18	R5:X4 612 72	R5 2,908 31 2,306	46 X4 43	R5:X4 67 63	R5 13,997 73 12, 1 39	47 X4 52	R5:X4 269.17	R5 24,377 59 16,045	48 X4 34	R5:X 716.9
No Drug RLU L83 RLU AMD RLU	R5 9,254 43 2,219	55 X4 23,846 9,150 40	R5:X4 0 39	R5 5,249 38 784	56 X4 20,393 8,290 38	R5:X4 0 26	R5 470 37 310	57 X4 39	R5:X4 12 05	R5 19, 17 5 96 19,638	58 X4 126 183 35	R5:X4 152 18	R5 513 35 500	59 X4 31	R5:X4 16.55	R5 3,264 30 3,038	60 X4 28	R5:X 4
No Drug RLU L83 RLU AMD RLU	R5 3,853 39 2,108	67 X4 77	R5:X4 50 04	R5 411 22 253	68 X4 34	R5:X4 12 09	R5 7,857 42 4,595	69 X4 41	R5:X4 191 63	R5 25,437 35 14,749	70 X4 38	R5:X4 669.39	R5 17,443 40 13,708	71 X4 45	R5:X4 387 62	R5 16,707 104 12,486	72 X4 38	R5:X 439 6
No Drug RLU L83 RLU AMD RLU	R5 263 33 143	79 X4 38	R5:X4 6 92	R5 3,890 44 986	80 X4 9,577 6,140 45	R5:X4 0 41	R5 2,089 33 1,105	81 X4 1,698 1,224 160	R5:X4 1 23	R5 475 30 159	82 X4 43	R5:X4 11.05	R5 8,475 30 6,862	83 X4 38	R5:X4 223 03	R5 4,107 28 2,571	84 X4 33	R5:X4 124.4
No Drug RLU L83 RLU AMD RLU	R5 443 33 451	91 X4 13,452 12,051 51	R5:X4 0 03	R5 34	92 X4 128,238 85,018 45	R5:X4 0.00	R5 22	93 X4 62	R5:X4	R5 45	94 X4 33	R5:X4	R5 43	95 X4 42	R5:X4	R5 46	96 X4 35	R5:X4



		21	
	R5	X4	R5:X4
no drug			
R5 inhibitor			
X4 inhibitor		i	
%inhib by R5 inhibitor			· · · · · · · · · · · · · · · · · · ·
%inhib by X4 inhibitor		i-	





		76	
	R5	X4	R5:X4
no drug	14,982	12,020	1
R5 inhibitor	111	10,839	
X4 inhibitor	8,580	3,384	
%inhib by R5 inhibitor	99	10	
%inhib by X4 inhibitor	43	72	

		95	
	R5	X4	R5:X4
no drug R5 inhibitor X4 inhibitor %inhib by R5 inhibitor %inhib by X4 inhibitor	43	42	

Table 4°C

Plate	1	Repeat 1	End time 6:39:36 PM	Start temp. 21 6	End temp. 21 7							
0.5 CPS	S (CF	PS)										
	18	-,										
266 192		54 262			7158 3 47 8	38 3946	1386 5010	930 46	100 14	1184 11004	112 7474	30488 60
1	106	9038	4002	32	238	26	976	34	38	48	9736	32
	38 122	2000 2984			16 38	36 20	298	52 15340	14 44	54 156	52 40	38 32
	36	2964 52			38 28	40	23344 62	15340 32	38	22	40	28
	22	32	28	9858	68	3802	46	11470	1958	42	42	24
	30	64	36	3846	3390	57858	12620	126186	68	34	38	36
Plate	2 2	Repeat 1	End time 6:41:51 PM	Start temp 21.5	End temp. 21 6							
0.5 CPS	S (CF 34	PS)										
262	94	56	6728	38882	7514	24	1048	1326	40	1134	82	27748
189		190			4418	4714	5398	58	26	10708	6786	40
	30 40	15002 2620			246 28	44 86	972 378	30 38	28 22	42 32	9654 52	30 30
	92	5434	9638	36	42	38	24348	25446	34	96	22	24
	44 30	44 44			46 142		92 30	36 7684	44 1438	54 44	46 34	48 42
	36	54			3840		14284	130290	56	32	46	34
Plate	, F	Repeat 1	End time 6:44:06 PM	Start temp 21.6		BarCode N/A						
0.5 CPS	S (CI 16	PS)										
185	90	18	4306	23902	5386	30	924	894	32	660	48	23382
	98	148			2880		3160	40	46	7616	2842	32
	30 28	10252 2396			172 26		842 172	30 32	32 22	44 28	7616 36	34 26
	64	3784			28		6188	5702	34	120	34	24
	16	28			28		38	38	38	44	62	34
	38 32	52 50			68 3138		62 13088	7324 104608	1076 32	50 38	42 50	32 32
Plate	4	Repeat 1	End time 6:46:20 PM	Start temp 21.7		BarCode N/A						
0.5 CP	4	1										
0.5 CP	4 S (CI 24	1 PS)	6:46:20 PM	21.7	21.8	N/A	704	974	32	862	44	21176
0.5 CP	4 S (CI 24 926	1 PS) 46 158	6:46:20 PM	21.7 27182 15882	21.8 5550 3026	N/A 26 2694	704 2956	974 26	32 20	862 5294	44 4906	21176 44
0.5 CPS 199 112	4 S (CI 24 926 214 56	1 PS) 46 158 11426	6:46:20 PM 5086 42 3252	21.7 27182 15882 82	21.8 5550 3026 270	26 2694 52	2956 814	26 36	20 40	5294 64	4906 6906	44 32
0.5 CPS 199 112	4 S (CI 24 926 214	1 PS) 46 158	6:46:20 PM 5086 42 3252 556	21.7 27182 15882 82 42	21.8 5550 3026	26 2694 52 64	2956	26	20	5294	4906	44
0.5 CP3 199 112	4 S (CI 24 926 214 56 32 72 32	1 PS) 46 158 11426 2916 3220 48	5086 42 3252 556 7618	21.7 27182 15882 82 42 36 30	21.8 5550 3026 270 30 38 28	N/A 26 2694 52 64 44 24	2956 814 242 12112 136	26 36 38 10878 30	20 40 24 32 56	5294 64 36 246 34	4906 6906 42 32 24	44 32 40 42 24
0.5 CP\$	4 S (CI 24 926 214 56 32 72 32 32	1 PS) 46 158 11426 2916 3220 48 38	6:46:20 PM 5086 42 3252 556 7618 22 40	21.7 27182 15882 82 42 36 30 8844	21.8 5550 3026 270 30 38 28	N/A 26 2694 52 64 44 24 2386	2956 814 242 12112 136 54	26 36 38 10878 30 4956	20 40 24 32 56 1372	5294 64 36 246 34 50	4906 6906 42 32 24 46	44 32 40 42 24 28
0.5 CP\$	4 S (CI 24 926 214 56 32 72 32 32 22	1 PS) 46 158 11426 2916 3220 48 38 34	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time	27182 15882 15882 42 36 30 8844 3498 Start temp.	21.8 5550 3026 270 30 38 28 2754 End temp.	N/A 26 2694 52 64 44 24 2386 59808 BarCode	2956 814 242 12112 136	26 36 38 10878 30	20 40 24 32 56	5294 64 36 246 34	4906 6906 42 32 24	44 32 40 42 24
0.5 CPS 199 112 Plate	4 S (CI 24 926 214 56 32 72 32 32 22	198) 46 158 11426 2916 3220 48 38 34 Repeat	6:46:20 PM 5086 42 3252 556 7618 22 40	27182 15882 15882 42 36 30 8844 3498 Start temp.	21.8 5550 3026 270 30 38 28 2754 End temp.	N/A 26 2694 52 64 44 24 2386 59808	2956 814 242 12112 136 54	26 36 38 10878 30 4956	20 40 24 32 56 1372	5294 64 36 246 34 50	4906 6906 42 32 24 46	44 32 40 42 24 28
0.5 CPS 199 112 Plate	4 S (CI 24 926 214 56 32 72 32 32 22 F 5 S (CI 38	19PS) 466 1588 11426 2916 3220 48 38 34 Repeat 1	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM	27182 27182 15882 82 36 30 8844 3498 Start temp.	21.8 5550 3026 270 30 38 28 86 2754 End temp.	26 2694 52 64 44 24 2386 59808 BarCode N/A	2956 814 242 12112 136 54 11014	26 36 38 10878 30 4956 65428	20 40 24 32 56 1372 34	5294 64 36 246 34 50 40	4906 6906 42 32 24 46 24	44 32 40 42 24 28 18
0.5 CPS 199 112 Plate	4 S (CI 24 926 214 56 32 72 32 32 22 F 5 S (CI 38	1 PS) 46 158 11428 2916 3220 48 38 34 Repeat 1	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM	21.7 27182 15882 15882 42 36 30 8844 3498 Start temp. 21 9	21.8 5550 3026 270 30 38 28 2754 End temp. 21.9	26 2694 52 64 44 2386 59808 BarCode N/A	2956 814 242 12112 136 54 11014	26 36 38 10878 30 4956 65428	20 40 24 32 56 1372 34	5294 64 36 246 34 50 40	4906 6906 42 32 24 46 24	44 32 40 42 24 28 18
0.5 CPS 199 112 Plate	4 S (CI 24 926 214 56 32 72 32 32 22 F 5 S (CI 38	19PS) 466 1588 11426 2916 3220 48 38 34 Repeat 1	6:46:20 PM 5086 42 3252 556 7618 22 40 End time 6.48 35 PM	21.7 27182 15882 82 42 36 30 8844 3498 Start temp. 21 9	21.8 5550 3026 270 30 38 28 86 2754 End temp.	26 2694 52 64 44 234 59808 BarCode N/A	2956 814 242 12112 136 54 11014	26 36 38 10878 30 4956 65428	20 40 24 32 56 1372 34	5294 64 36 246 34 50 40	4906 6906 42 32 24 46 24	44 32 40 42 24 28 18
0.5 CPS	4 S (CI 24 926 214 56 32 72 32 32 22 F 5 S (CI 38 38 26 42 28	1 PS) 46 158 11426 2916 3220 48 38 34 Repeat 1 PS)	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM	21.7 27182 15882 15882 36 30 8844 3498 Start temp. 21 9 976 530	21.8 55550 3026 270 30 38 28 2754 End temp, 21.9 38 190 36	N/A 26 2694 52 64 44 24 2386 59808 BarCode N/A 234 58 34	2956 814 242 12112 136 54 11014 46 46 102 40	26 36 38 10878 30 4956 65428	20 40 24 32 56 1372 34 46 28 34 54	5294 64 36 246 34 50 40 30 2298 24 26	4906 6906 42 32 24 46 24 46 24 1290 40 30	22 22 26 28 18
0.5 CPS	4 S (CI 24 926 214 56 32 72 32 32 22 22 F 5 S (CI 38 38 26 42 28 36	19PS) 466 1588 11426 2916 3220 48 3220 48 38 34 Repeat 1 PS) 28 20 3260 378 62	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM 40 32 420 88 11690	21.7 21.7 27182 15882 82 42 36 30 8844 3498 Start temp. 21 9 6 50 50 32 388	21.8 5550 3026 270 38 28 2754 End temp. 21.9 38 190 36 34	26 2694 52 64 44 2386 59808 BarCode N/A	2956 814 242 12112 136 54 11014	26 36 38 10878 30 4956 65428	20 40 24 32 56 1372 34 46 28 34 54 54	5294 64 36 246 34 50 40 30 2298 24 26 30 30 30 30 30 30 30 30 30 30 30 30 30	4906 6906 42 32 24 46 24 34 1290 40 30 46	22 26 24 28 18
0.5 CPS	4 S (CI 24 926 214 56 32 72 32 32 22 F 5 S (CI 38 38 26 42 28 36 46 22	1 PS) 466 158 11428 2916 3220 48 38 34 Repeat 1 PS) 28 20 3266 378 62 328	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM 40 32 420 88 11690 44	21.7 27182 15882 15882 36 30 8844 3498 Start temp. 21 9 30 976 50 32 38 38 38	21.8 55550 3026 2707 30 38 28 2754 End temp, 21.9 38 190 34 44 44 58	N/A 26 2694 52 64 44 2386 59808 BarCode N/A 234 32 32 32 26	2956 814 242 12112 136 54 11014 46 46 40 40 42 38 34	26 36 38 10878 30 4956 65428 30 24 26 42 42 42 30 50	20 40 24 32 56 1372 34 46 28 34 54 26 32 200	5294 64 36 246 34 50 40 30 2298 24 26 36 36 36	4906 6906 42 32 24 46 24 34 1290 40 30 46 38 38	44 32 40 42 24 28 18 22 26 24 48 42 12 36
0.5 CPS	4 S (CI 24 926 214 56 32 72 32 32 22 F 5 S (CI 38 38 38 26 42 28 36 46	1 PS) 466 158 11428 2916 3220 48 38 34 Repeat 1 PS) 28 20 3260 378 62 22	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM 40 32 420 88 11690 44	21.7 27182 15882 15882 36 30 8844 3498 Start temp. 21 9 30 976 50 32 38 38 38	21.8 5550 3026 270 30 38 28 2754 End temp. 21.9 38 1990 36 34 44	N/A 26 2694 52 64 44 2386 59808 BarCode N/A 234 32 32 32 26	2956 814 242 12112 136 54 11014 46 46 102 40 42 38	26 36 38 10878 30 4956 65428	20 40 24 32 56 1372 34 46 28 34 54 26 32	5294 64 36 246 34 50 40 30 2298 24 26 36 36	4906 6906 42 32 24 46 24 1290 40 30 46 38	44 32 40 42 24 28 18
0.5 CPS	4 S (CI 24 214 56 32 72 32 32 22 F 5 S (CI 38 38 26 42 28 36 46 22 36	1 PS) 460 158 11426 2916 3220 48 38 34 Repeat 1 PS) 28 20 3266 378 62 22 38 80 Repeat	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM 40 32 420 88 11690 44	21.7 27182 27182 15882 36 30 8844 3498 Start temp. 21 9 30 976 50 30 38 40 Start temp	21.8 5550 3026 270 30 38 28 2754 End temp, 21.9 38 190 36 34 44 58 42 36	26 2694 52 64 44 24 2386 59808 BarCode N/A	2956 814 242 12112 136 54 11014 46 46 40 40 42 38 34	26 36 38 10878 30 4956 65428 30 24 26 42 42 42 30 50	20 40 24 32 56 1372 34 46 28 34 54 26 32 200	5294 64 36 246 34 50 40 30 2298 24 26 36 36 36	4906 6906 42 32 24 46 24 34 1290 40 30 46 38 38	44 32 40 42 24 28 18 22 26 24 48 42 12 36
0.5 CPS	4 S (CI 24 926 214 56 32 72 32 32 22 5 S (CI 38 38 26 42 28 36 46 22 36	1 PS) 466 158 11428 2916 3220 48 38 34 Repeat 1 PS) 28 20 3260 378 62 22 38 80 Repeat	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM 40 32 420 88 11690 11690 44 52 52 End time	21.7 27182 27182 15882 36 30 8844 3498 Start temp. 21 9 30 976 50 30 38 40 Start temp	21.8 5550 3026 270 30 38 28 2754 End temp, 21.9 38 190 36 34 44 58 42 36	26 2694 52 64 44 2386 59808 BarCode N/A	2956 814 242 12112 136 54 11014 46 46 40 40 42 38 34	26 36 38 10878 30 4956 65428 30 24 26 42 42 42 30 50	20 40 24 32 56 1372 34 46 28 34 54 26 32 200	5294 64 36 246 34 50 40 30 2298 24 26 36 36 36	4906 6906 42 32 24 46 24 34 1290 40 30 46 38 38	44 32 40 42 24 28 18 22 26 24 48 42 12 36
0.5 CPS 199 112 Plate 0.5 CPS	4 S (CI 24 926 214 56 32 72 32 32 32 22 25 5 S (CI 38 46 42 28 36 46 22 36 5 6 S (Ci 30 46 21 46 46 46 46 46 46 46 46 46 46 46 46 46	1 PS) 46 158 11428 2916 3220 48 38 34 Repeat 1 PS) 28 20 3260 378 62 22 38 80 Repeat 1 PS)	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM 40 32 420 88 11690 44 52 52 End time 6 50.50 PM	21.7 27182 27182 15882 36 30 8844 3498 Start temp. 21 9 650 650 632 640 540 Start temp. 21 8	21.8 5550 3026 270 30 38 86 2754 End temp. 21.9 36 34 44 58 42 36 End temp. 21 9	26 2694 52 64 44 24 2386 59808 BarCode N/A	2956 814 242 12112 136 54 11014	26 36 38 10878 30 4956 65428	20 40 24 32 56 1372 34 46 28 34 54 26 32 2000 22	5294 64 36 246 34 50 40 2298 24 26 36 36 40	4906 6906 42 32 24 46 24 1290 40 30 46 38 34 42	24 28 18 22 24 28 18 22 26 24 48 42 21 36 36
0.5 CPS 199 112 Plate 0.5 CPS	4 S (CI 24 926 214 556 32 72 32 32 22 5 5 S (CI 38 38 42 28 36 42 28 36 42 36 5 (CI 30 30 26 42	1 PS) 468 158 11426 2916 3220 48 38 34 Repeat 1 PS) 28 20 3260 378 62 22 22 22 28 Repeat 1 PS)	6:46:20 PM 5086 42 3252 556 7618 22 40 End time 6.48 35 PM 40 32 420 88 11690 44 52 52 End time 6 50.50 PM	21.7 27182 15882 15882 42 36 36 38 44 3498 Start temp. 21 9 30 976 50 32 38 38 40 0 Start temp 21 8	21.8 5550 3026 270 30 38 86 2754 End temp. 21.9 36 34 44 58 42 36 End temp. 21 9	26 2694 52 64 44 2386 59808 BarCode N/A 234 58 34 32 26 64 40 BarCode N/A	2956 814 242 12112 136 54 11014 46 46 46 102 40 42 38 34 52	26 36 38 10878 30 4956 65428 30 24 26 42 42 42 30 50 54	20 40 24 32 56 1372 34 46 28 34 54 54 26 32 200 22	5294 64 366 246 34 500 40 30 2298 24 26 36 36 36 40	4906 6906 42 32 24 46 66 24 34 1290 40 30 46 38 34 42	44 32 40 42 24 28 18 18 22 26 24 48 42 12 36 36
0.5 CPS 199 112 Plate 0.5 CPS	4 S (Cl 24 926 214 556 32 72 32 32 22 5 S (Cl 38 38 26 42 28 36 6 S (Cl 30 6 5 6 6 8 8 9 6 9 9 9 9 9 9 9 9 9 9 9 9 9 9	1 PS) 466 158 11428 2916 3220 48 38 34 Repeat 1 PS) 28 20 3260 378 62 22 38 80 Repeat 1 PS)	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM 40 32 420 88 11690 44 52 End time 6 50.50 PM	21.7 27182 27182 15882 36 30 8844 3498 Start temp. 21 9 30 976 50 32 38 38 40 21 40 Start temp 21 8	21.8 5550 3026 270 30 38 86 2754 End temp. 21.9 36 34 44 42 36 End temp. 21 9	26 2694 52 64 44 24 2386 59808 BarCode N/A	2956 814 242 12112 136 54 11014 46 46 102 40 42 23 38 34 52	26 36 36 10878 30 4956 65428 30 24 26 42 42 42 42 50 50 54	20 40 24 32 56 1372 34 46 28 34 54 26 32 200 22	5294 64 36 246 34 50 40 2298 24 26 36 36 40 36 2268 56 53	4906 6906 42 32 24 46 24 1290 40 30 46 38 34 42	44 32 40 42 24 28 18 18 22 26 24 48 42 22 36 36 36
0.5 CPS 199 112 Plate 0.5 CPS	4 S (CI 24 24 22 32 22 5 S (CI 38 38 26 46 22 36 46 22 36 46 22 36 46 22 36 46 22 36 46 22 36 30 26 42 36 32 36	11 PS) 468 158 11426 2916 3220 48 38 34 Repeat 1 PS) 28 20 3260 378 62 22 22 22 38 80 Repeat 1 PS)	6:46:20 PM 5086 42 3252 556 7618 22 40 End time 6.48 35 PM 40 32 420 88 11690 44 52 End time 6 50.50 PM	21.7 27182 15882 15882 36 36 38 44 3498 Start temp. 21 9 30 30 976 50 32 33 38 40 40 Start temp 21 8	21.8 5550 3026 270 30 38 86 2754 End temp. 21.9 36 34 44 58 42 36 End temp. 21 9	26 2694 52 64 44 2386 59808 BarCode N/A 234 58 34 32 26 64 40 BarCode N/A 8 34 40 34 34 40 38 34 40 34 34 34 40 34 34 34 34 34 34 34 34 34 34 34 34 34	2956 814 242 12112 136 54 11014 46 46 102 40 42 38 34 52	26 36 38 10878 30 4956 65428 30 24 26 42 42 42 30 50 54	20 40 24 32 56 1372 34 46 28 34 54 56 32 200 22	5294 64 366 246 34 500 40 30 2298 24 26 36 36 36 40 36 2288 56 34 34 34 34	4906 6906 42 32 24 46 66 24 34 1290 40 30 46 38 34 42	44 32 40 42 24 28 18 18 22 26 24 48 42 12 36 36 36
0.5 CPS 199 112 Plate 0.5 CPS	4 S (Cl 24 926 214 556 32 72 32 32 22 5 S (Cl 38 38 26 42 28 36 6 S (Cl 30 6 S (Cl 30 6 8 S (Cl 30 8 S (Cl 30	1 PS) 466 158 11428 2916 3220 48 38 34 Repeat 1 PS) 28 20 3260 378 62 22 38 80 Repeat 1 PS)	6:46:20 PM 5086 42 3252 556 7618 22 40 40 End time 6.48 35 PM 40 32 420 420 420 52 End time 6 50.50 PM	21.7 27182 27182 15882 82 42 36 30 8844 3498 Start temp. 219 30 976 50 32 38 40 40 Start temp 218 40 Start temp	21.8 5550 3026 270 30 38 28 86 2754 End temp. 21.9 40 118 44 44 41 41 42 30	26 2694 52 64 44 2346 59808 BarCode N/A 32 32 32 26 40 BarCode N/A 550 38 34 40 34 32 34 34 34 34 34 34 34 34 34 34 34 34 34	2956 814 242 12112 136 54 11014 46 46 102 40 42 23 38 34 52	26 36 36 10878 30 4956 65428 30 24 26 42 42 42 42 50 50 54	20 40 24 32 56 1372 34 46 28 34 54 26 32 200 22	5294 64 36 246 34 50 40 2298 24 26 36 36 40 36 2268 56 53	4906 6906 42 32 24 46 24 1290 40 30 46 38 34 42	44 32 40 42 24 28 18 22 26 24 48 42 12 36 36 36



Plate 1	Repeat 1	End time #######	Start temp. 21 7	End temp. 21 8							
0.5 CPS (C	:PS)										
32											
24	14218	56	21586	28	4034	36	52	42088	40	43332	38
4780 69452	174 15306	71276 4008	730 44	48 792	326 180	28 50	12022 182	1288 25292	7198 718	4314 3572	17856 424
72	3922	546	128	44	66	30	900	11984	3194	16106	23794
30	88	18820	40438	4882	105946	8466	4934	470	20386	548	3376
3420 344	934 82	344 5344	6268 5330	5012 6710	170 1880	3546 338	504 4286	8164 2112	22214 466	15146 7752	19592 4078
580	1018	516	318	302	40	414	32	20	52	48	42
Diete	Dancet	Cad topo	Ctool town	Food towns	ParCada						
Plate 2	Repeat 1	End time #######	Start temp 21 9	21 9							
0.5 CPS (C	·DC/										
22											
44	14062	36	21726	32	3942	24	46	42324	50	45846	26
4324	124	63502	492	44	242	172	10576	1258	7552	4480	14374
66204	14658	3568	56	524	282	56	172	24186	506	2422	408
128 40	3526 78	354 17378	168 38076	20 5944	54 89520	60 10042	528 5564	10074 470	2622 17964	11888 478	24960 3152
4118	638	336	4110	3624	222	4160	318	7550	28660	19740	13822
438	114	3554	3384	5470	1892	188	3494	2066	484	9198	4136
440	940	466	282	292	38	472	36	24	38	38	50
	Repeat	End time	Start temp.								
3	1	########	21.9	22	N/A						
0.5 CPS (C	PS)										
36											
36	38			38	28	36	42	114	40	60	46
32 126		80 34	26 42	16 30	36 46	30 22	18 26	26 32	30 58	48 8	80 28
26				34	20	18	34	24	36	100	60
28				32	26	42	52	36	106	34	24
34 38			24 36	32 80	18 50	38 38	18 44	36 34	38 38	50 30	58 28
40			30	24	22	38	36	34	36	22	26
Plate	Reneat	End time	Start temp	End temp	BarCode						
Plate 4	Repeat 1	End time	Start temp 21.9		BarCode N/A						
4	. 1										
	:PS)										
0.5 CPS (C 16	(PS)	#######################################	21.9	22	N/A	18	32	66	30	60	34
4 0.5 CPS (C 16 24 24	1 CPS) 70 46	######################################	21.9 26 34	22 26 26	N/A 40 40	18 34	32 26	66 26	30 50	60 36	34 56
4 0.5 CPS (C 16 24 24 132	70 70 46 116	30 118 84	21.9 26 34 34	26 26 34	N/A 40 40 48	34 34	26 38	26 30	50 38	36 36	56 28
4 0.5 CPS (C 16 24 24	70 46 116 30	30 118 84 32	21.9 26 34 34 28	22 26 26	N/A 40 40	34	26	26	50	36	56
4 0.5 CPS (C 16 24 24 132 32 34 24	70 46 116 30 84 28	30 118 84 32 12036 42	21.9 26 34 34 28 94 44	26 26 26 34 26 38 24	N/A 40 40 48 40 34 28	34 34 46 44 40	26 38 28 24 26	26 30 12 38 48	50 38 26 86 32	36 36 46 36 30	56 28 58 36 150
4 0.5 CPS (C 16 24 24 132 32 34 24 62	70 46 116 30 84 28 24	30 118 84 32 12036 42 58	21.9 26 34 34 28 94 44 32	26 26 26 34 26 38 24 66	N/A 40 40 48 40 34 28 26	34 34 46 44 40 28	26 38 28 24 26 44	26 30 12 38 48 32	50 38 26 86 32 22	36 36 46 36 30 30	56 28 58 36 150 28
4 0.5 CPS (C 16 24 24 132 32 34 24	70 46 116 30 84 28 24	30 118 84 32 12036 42 58	21.9 26 34 34 28 94 44 32 28	26 26 34 26 38 24 66 40	N/A 40 40 48 40 34 28 26 28	34 34 46 44 40	26 38 28 24 26	26 30 12 38 48	50 38 26 86 32	36 36 46 36 30	56 28 58 36 150
4 0.5 CPS (C 16 24 132 32 34 24 62 44 Plate	70 46 116 30 84 28 24 80 Repeat	30 118 84 32 12036 42 58 60	21.9 26 34 34 28 94 44 32 28 Start temp.	26 26 26 34 26 38 24 66 40 End temp	N/A 40 40 48 40 34 28 26 28 BarCode	34 34 46 44 40 28	26 38 28 24 26 44	26 30 12 38 48 32	50 38 26 86 32 22	36 36 46 36 30 30	56 28 58 36 150 28
4 0.5 CPS (C 16 24 24 132 32 34 24 62	70 46 116 30 84 28 24 80 Repeat	30 118 84 32 12036 42 58 60	21.9 26 34 34 28 94 44 32 28	26 26 26 34 26 38 24 66 40 End temp	N/A 40 40 48 40 34 28 26 28	34 34 46 44 40 28	26 38 28 24 26 44	26 30 12 38 48 32	50 38 26 86 32 22	36 36 46 36 30 30	56 28 58 36 150 28
4 0.5 CPS (C 16 24 24 132 32 34 44 Plate 5 0.5 CPS (C	70 46 116 300 84 28 24 80 Repeat 1	30 118 84 32 12036 42 58 60	21.9 26 34 34 28 94 44 32 28 Start temp.	26 26 26 34 26 38 24 66 40 End temp	N/A 40 40 48 40 34 28 26 28 BarCode	34 34 46 44 40 28	26 38 28 24 26 44	26 30 12 38 48 32	50 38 26 86 32 22	36 36 46 36 30 30	56 28 58 36 150 28
4 0.5 CPS (C 16 24 24 132 32 34 24 62 44 Plate 0.5 CPS (C 34	70 46 116 30 84 80 80 Repeat 1	30 118 84 32 12036 60 End time	21.9 26 34 34 28 94 44 32 28 Start temp.	26 26 34 26 38 24 66 40 End temp	40 40 48 40 34 28 26 28 BarCode N/A	34 34 46 44 40 28 28	26 38 28 24 26 44 34	26 30 12 38 48 32 32	50 38 26 86 32 22 36	36 36 46 36 30 30 18	56 28 58 36 150 28 28
4 0.5 CPS (C 16 24 24 132 32 34 62 44 Plate 5 0.5 CPS (C 34 38 38 38 38 38 38 5 CPS (C 34 38 38 38 5 CPS (C 34 38 38 38 38 38 5 CPS (C 34 38 38 38 38 38 38 5 CPS (C 34 38 38 38 38 38 38 38 5 CPS (C 34 38 38 38 38 38 38 38 38 38 38 38 38 38	70 464 30 844 80 Repeat 1 CPS)	30 118 84 32 12036 60 End time #######	21.9 26 34 34 28 94 42 28 Start temp. 22	26 26 34 26 38 24 66 40 End temp 22	40 40 48 40 34 28 26 28 BarCode N/A	34 34 46 44 40 28 28	26 38 28 24 26 44 34	26 30 12 38 48 32 32 32	50 38 26 86 32 22 36	36 36 46 36 30 30 18	56 28 58 36 150 28 28
9 0.5 CPS (C 16 24 24 132 32 34 24 62 44 Plate 5 0.5 CPS (C 34 38 762	70 464 116 300 844 800 Repeat 1 1 1 1 1 2 PS)	30 118 84 32 12036 42 58 60 End time ########	21.9 26 34 34 28 94 44 32 28 Start temp.	26 26 26 34 26 38 24 66 40 End temp 22	40 40 48 40 34 28 26 8 BarCode N/A	34 34 46 44 40 28 28 28	26 38 28 24 26 44 34	26 30 12 38 48 32 32 32	50 38 26 86 32 22 36	36 36 46 36 30 30 18	56 28 58 36 150 28 28
4 0.5 CPS (C 16 24 24 132 32 34 24 62 44 Plate 5 0.5 CPS (C 34 38 762 52058 106	70 464 1166 30 844 80 80 80 80 80 80 80 80 80 80 80 80 80	30 118 84 32 12036 60 End time ####### 26 39888 5224 172	21.9 26 34 34 28 94 44 32 28 Start temp. 22 6696 88 600 170	26 26 34 26 38 24 66 40 End temp 22	40 40 48 40 34 28 26 28 BarCode N/A	34 34 46 44 40 28 28 28	26 38 28 24 26 44 34 40 8416 340 444	26 30 12 38 48 32 32 32 29548 1262 22410 7478	50 38 26 86 32 22 36 40 409 534 2458	36 36 46 36 30 30 18 30628 1598 1046	56 28 58 36 150 28 28 34 12372 512 15470
9 0.5 CPS (C 16 24 24 132 32 34 24 62 44 Plate 5 0.5 CPS (C 34 38 762 52058 106 30 30	70 464 116 300 844 84 84 84 84 88 85 86 24 80 86 86 86 86 86 86 86 86 86 86 86 86 86	30 118 84 32 12036 42 58 60 End time ######## 266 39888 2524 172 16428	21.9 26 34 34 28 94 44 32 28 Start temp. 22 6696 88 60 1700 25792	26 26 26 34 26 38 24 66 40 End temp 22 34 40 450 38 4240	40 40 48 40 34 28 26 28 BarCode N/A	34 34 46 44 40 28 28 44 36 32 30 2092	26 38 28 24 26 44 34 34 40 8416 340 444 4630	26 30 12 38 48 32 32 32 29548 1262 22410 7478 334	50 38 26 86 32 22 36 40 4096 534 2458 17130	36 36 46 36 30 30 18 30628 1598 1046 10024 388	56 28 58 36 150 28 28 34 12372 512 15470 2730
4 0.5 CPS (C 16 24 24 132 32 34 24 62 44 Plate 5 0.5 CPS (C 34 38 762 52058 106	70 46 116 30 84 80 80 80 24 80 80 20 80 46 732	30 118 84 32 12036 60 End time ######## 266 39888 2524 172 16428 358	21.9 26 34 34 44 32 28 Start temp. 22 6696 88 80 170 25792 5044	26 26 34 26 38 24 66 40 End temp 22	40 40 48 40 34 28 26 28 BarCode N/A	34 34 46 44 40 28 28 28	26 38 28 24 26 44 34 40 8416 340 444	26 30 12 38 48 32 32 32 29548 1262 22410 7478	50 38 26 86 32 22 36 40 409 534 2458	36 36 46 36 30 30 18 30628 1598 1046	56 28 58 36 150 28 28 34 12372 512 15470
4 0.5 CPS (C 16 24 24 132 32 34 24 62 44 Plate 5 0.5 CPS (C 34 38 762 52058 106 30 2498	70 464 1166 30 844 80 80 865 2080 46 7323 300	300 118 84 32 12036 60 End Irrne ######### 26 39888 2524 172 16428 3986 3986 3986	21.9 26 34 34 28 94 44 32 28 Start temp. 22 6696 88 60 170 25792 5044 886	26 26 34 26 38 24 66 40 End temp 22 34 40 450 38 4240 3236	AU 40 40 48 40 40 48 28 26 28 BarCode N/A 3960 30 168 38 45094 202	34 34 46 64 40 28 28 28 44 36 32 30 2092 2124	26 38 28 24 26 44 34 40 8416 340 444 630 292	26 30 12 38 48 32 32 29548 1262 22410 7478 334 4806	50 38 26 86 32 22 23 36 40 4096 534 2458 17130 13736	36 36 46 36 30 30 30 18 30628 1598 1046 10024 388 13012	56 28 58 36 150 28 28 28 34 12372 512 15470 2730 12386
4 0.5 CPS (C 16 24 24 132 32 34 24 62 44 Plate 0.5 CPS (C 34 38 762 52058 106 30 2498 290	70 464 1166 30 844 80 80 80 80 46 7323 30 816 Repeat	300 118 84 32 12036 60 End time ######## 26 39888 2524 172 16428 3886 438 End time	21.9 26 34 34 28 94 44 32 28 Start temp. 22 6696 88 60 170 25792 5044 886 294 Start temp	26 26 34 26 38 24 66 40 End temp 22 34 40 450 38 4240 3236 4584 260	40 40 48 40 34 28 26 28 BarCode N/A 3960 30 168 38 45094 44	34 34 46 64 40 28 28 28 44 36 32 30 2092 2124 110	26 38 28 24 26 44 34 40 8416 340 444 630 292 940	26 30 12 38 48 32 32 32 29548 1262 22410 7478 334 4806 1286	50 38 26 86 32 22 36 40 409 6534 2458 17130 13736 162	36 36 46 36 30 30 18 30628 1598 1046 10024 388 13012 6768	56 28 58 36 150 28 28 34 12372 512 15470 2730 12386 2204
90.5 CPS (C) 16 24 24 132 32 34 24 62 44 Plate 5 0.5 CPS (C) 34 38 762 52058 106 30 2498 290 456	70 464 1166 30 844 80 80 80 80 46 7323 30 816 Repeat	30 118 84 32 12036 42 58 60 End time ######## 266 39888 2524 172 16428 3986 438	21.9 26 34 34 44 32 8 Start temp. 22 6696 88 60 170 25792 5044 886 294	26 26 34 26 38 24 66 40 End temp 22 34 40 450 38 4240 3236 4584 260	AU 40 40 48 40 34 428 26 28 BarCode N/A 3960 30 168 38 45094 202 240 44 BarCode	34 34 46 64 40 28 28 28 44 36 32 30 2092 2124 110	26 38 28 24 26 44 34 40 8416 340 444 630 292 940	26 30 12 38 48 32 32 32 29548 1262 22410 7478 334 4806 1286	50 38 26 86 32 22 36 40 409 6534 2458 17130 13736 162	36 36 46 36 30 30 18 30628 1598 1046 10024 388 13012 6768	56 28 58 36 150 28 28 34 12372 512 15470 2730 12386 2204
4 0.5 CPS (C 16 24 132 32 34 24 62 44 Plate 5 0.5 CPS (C 34 38 762 52058 106 30 2498 290 456 Plate 6 0.5 CPS (C	70 46 116 30 84 80 80 80 80 80 80 80 80 80 80 80 80 80	300 118 84 32 12036 60 End time ######## 26 39888 2524 172 16428 3886 438 End time	21.9 26 34 34 28 94 44 32 28 Start temp. 22 6696 88 60 170 25792 5044 886 294 Start temp	26 26 34 26 38 24 66 40 End temp 22 34 40 450 38 4240 3236 4584 260	AU 40 40 48 40 34 428 26 28 BarCode N/A 3960 30 168 38 45094 202 240 44 BarCode	34 34 46 64 40 28 28 28 44 36 32 30 2092 2124 110	26 38 28 24 26 44 34 40 8416 340 444 630 292 940	26 30 12 38 48 32 32 32 29548 1262 22410 7478 334 4806 1286	50 38 26 86 32 22 36 40 409 6534 2458 17130 13736 162	36 36 46 36 30 30 18 30628 1598 1046 10024 388 13012 6768	56 28 58 36 150 28 28 34 12372 512 15470 2730 12386 2204
9 0.5 CPS (C 16 24 24 132 32 34 24 62 44 Plate 5 0.5 CPS (C 34 38 762 52058 106 30 2498 290 456 Plate 6 6	70 46 116 30 84 80 80 80 80 80 80 80 80 80 80 80 80 80	300 118 84 32 12036 60 End time ######## 26 39888 2524 172 16428 3886 438 End time	21.9 26 34 34 28 94 44 32 28 Start temp. 22 6696 88 60 170 25792 5044 886 294 Start temp	26 26 34 26 38 24 66 40 End temp 22 34 40 450 38 4240 3236 4584 260	AU 40 40 48 40 34 428 26 28 BarCode N/A 3960 30 168 38 45094 202 240 44 BarCode	34 34 46 64 40 28 28 28 44 36 32 30 2092 2124 110	26 38 28 24 26 44 34 40 8416 340 444 630 292 940	26 30 12 38 48 32 32 32 29548 1262 22410 7478 334 4806 1286	50 38 26 86 32 22 36 40 409 6534 2458 17130 13736 162	36 36 46 36 30 30 18 30628 1598 1046 10024 388 13012 6768	56 28 58 36 150 28 28 34 12372 512 15470 2730 12386 2204
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		1,128	25	35	45	20,393	34	9,577	128,238		934	33	83	32	8,290	34	6,140	85,018		37	32	88	40	38	78	45	45
		1,217	5,204	974	338	3,846	77	38	3,452		814	3,058	828	207	9,150	87	28	2,051		45	34	92	59	40	34	33	21
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		45	7,375	612	2,908	19,175	5,437	475	42		35	4	48	31	96	32	33	36		4	3,961	479	2,306	19,638	14,749	159	28
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		21,656	611	20	148	39,257	5,189	4,357	300		27	30	38	33	82	34	34	29		7,226	9/	23	139	27,832	5,356	906	268
		46	37,389	3,788	450	660'81	340	4,449	491		58	66	29	37	13.896	3	43	49		32	12,295	2,049	206	16,980	282	3,752	376
		14,140	149	14,982	3.724	8	786	86	979		54	4	111	38	115	39	31	22			•	_		37			
R5	No Drug	34	4,552	67,828	100	38	3,769	391	510	L83	30	78	129	58	31	29	20	45	AMD	39	838	51,146	153	38	2,773	340	564

T20 Resistance Mutations

SDM Virus	T20 Sens.a	T20 FCb
HXB2 G I V		1.0
NL4-3 G I V	S	5.2
NL4-3 D I V	S	12.8
NL4-3 G I M	S	33.0
NL4-3 S I V	S	74.2
NL4-3 D I M	X	113.0
NL4-3 S I M	~	227.4
NL4-3 D T V	X	>281.8
JRCSF G I V		2.1
JRCSF D I V		104.0

^a Rimsky et al., J. Virol. 72(2):986-993

b Fold change in IC50 (vs. HXB2) using PhenoSense HIV Entry Assay

SDM Virus	T20 Sens.a	<u>T20_FC</u> b
HXB2 GIV		1.0
NL4-3 G I V	S	5.2
NL4-3 D I V	S	12.8
NL4-3 G I M	S	33.0
NL4-3 S I V	S	74.2
NL4-3 D I M	R	113.0
NL4-3 S I M	R	227.4
NL4-3 D T V	R	>281.8
JRCSF G I V		2.1
JRCSF D I V		104.0

Entry Inhibitor Susceptibility: T-20 Fusion Inhibitor

Drug resistance mutations were introduced into well-characterized X4 tropic (NL4-3) and R5 tropic (JRCSF) viruses. T20 susceptibility was measured using the virus entry assay. The fold change (FC) in T-20 susceptibility for each virus was determined by dividing the IC50 of the test virus by the IC50 of the HXB2 strain of HIV-1. T-20 sensitivity of similar mutant viruses has been reported in the scientific literature (Rimsky et al.,).

Identifying Entry Inhibitor Resistance Mutations

Virus			A/	4	sec	nt	านอ	AA Sequence ^a				
HXB2	Q			2	9		>	Q	Q	Q		
1	Q			S	9	Ι	>	Q	Q	Q		
2	Q			8		Ι		Ó	Q	Q		
3	Q			S	×	Η	×	Q	Q	Q	X=G/S	X=X
4	Q		T	S	9	Η	>	Ó	Q	Q		
5	Q	T		S	9	Τ	>	Ó	Q	Q		
9	Q			S	×	Ι	X	Ò	Q	Q	X=G/S	$\chi = \chi$
7	Q			S	9	Ι	\	Q	Q	Q		
8	Q			8	9	Ι	>	Q	Q	Q		
6	Q			S	g	Ι	\	Q	Q	Q		
10	Q			8		Ι	\	Q	Q	Q		
12	Q			8	×	I	\	Q	Q	Q	X=G/D	
13	ď			S	9	Н	>	Q	Q	Q		

a gp41 amino acid sequence positions 32 to 41

Virus	AA_Sequence ^a	
HXB2	QLLSGIVQQQ	
1	QLLSGIVQQQ	
2	QLLSSIMQQQ	
3	QLLSXIXQQQ X=G/S	X=V/M
4	QLLSGIVQQQ	
5	QLLSGIVQQQ	
6	QLLSXIXQQQ X=G/S	X=V/M
7	QLLSGIVQQQ	
8	QLLSGIVQQQ	
9	QLLSGIVQQQ	
10	QLLSDIVQQQ	
12	QLLSXIVQQQ X=G/D)
13	QLLSGIVQQQ	

Identifying Envelope Protein Mutations.

Viruses with reduced (or increased) susceptibility to an entry inhibitor are identified using the virus entry assay. Mutations that may confer reduced (or increased) susceptibility to the entry inhibitor are identified by sequencing the envelope genes of the sensitive and resistant viruses. The deduced amino acid sequences of the sensitive and resistant viruses are compared to identify candidate drug resistance mutations. The ability of a specific mutation to confer altered drug susceptibility is confirmed or disproved by introducing the mutation into a drug sensitive virus and measuring the susceptibility of the mutant virus in the virus entry assay. In the example represented here, a short stretch of amino acid sequences within the first heptad repeat (HR-1) of the HIV-1 gp41 transmembrane envelope protein is aligned for viruses exhibiting different T-20 susceptibilities. Highlighted amino acids represent mutations known to confer reduced susceptibility to T-20.

Similar analyses can be used to identify envelope amino acid sequences that (a) alter/influence susceptibility to CCR5 or CXCR4 inhibitors, (b) specify X4, R5 and dual tropism, and © elicit neutralizing antibodies.

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